CONSTRUCTION OF A PATIENT-SPECIFIC ATLAS OF THE BRAIN: APPLICATION TO NORMAL AGING

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ABSTRACT

We present a method for the construction of patient-specific atlases of the brain. Traditional atlases of the brain aim to characterize the variability of a population of subjects. A common approach is to average the anatomies of a population after alignment to a common coordinate system. Subjects are typically given equal weights during averaging which results in atlases that are population-specific rather than subject specific. In this paper we propose a method for the construction of patient-specific atlas for a given query subject from a large population cohort. During the atlas construction we compute the similarity between the query subject and the subjects in the population cohort. This similarity measure can be based on image similarity or other meta-information (e.g. sex, age, ethnicity, medical history, etc). We show an example of the construction of brain atlases for different ages using a cohort of 575 subjects between the ages of 18 and 80.

Index Terms— patient-specific atlas, 4D atlas, kernel smoothing, average space atlas

1. INTRODUCTION

The ability to construct a representative anatomical atlas of a given population is an important tool in the analysis and interpretation of medical images, enabling spatial characteristics, such as the size and location of structures, to be determined. For example, atlases of different populations can be compared to determine differences, or a subject can be compared to an atlas of normal anatomy in order to detect abnormalities or potential disease.

The creation and use of atlases requires bringing subjects in the population into a common coordinate system in which the subjects can be compared. How to define such a common space is a major topic of research, particularly in brain image analysis. One of the earliest atlases, and one which is still frequently used, is the Talairach atlas [1], which was constructed from imaging the post-mortem brain of one 60 year-old female. However, a single subject can never account for all the variation in a population, and the subject may not be representative of the group under consideration. This has motivated the development of population atlases, created from several subjects of the same population.

One approach creates probabilistic atlases which include information about the probability of certain anatomical structures from a set of subjects making them more representative of a population. These atlases have been successfully used to investigate structural and functional differences in the human brain as part of the International Consortium for Brain Mapping (ICBM) [2]. A prominent example of such a probabilistic atlas of the human brain is the atlas developed at the Montreal Neurological Institute (MNI) [3] where MR images from 305 subjects were mapped into stereotactic space, segmented and averaged on a voxel-by-voxel basis. Another approach generates atlases which describe the statistical variability of anatomical structures [4, 5, 6].

Both types of atlases are typically static in the sense that they are constructed from a pre-defined population. A notable exception to this is the dynamic brain atlas proposed by Hill et al. [7] in which a subject-specific probabilistic atlas is constructed by selecting different subgroups of the population. For their particular application the different subgroups are defined by the ages of the subjects in the population. However, each subject is given the same weight during the atlas construction. This ignores the fact that some subjects are more relevant for a particular query subject.

More recently Davis et al. [8] proposed a method for population-based shape regression. We adopt this idea to build a 4D atlas of the ageing brain which can be customized to a particular age of a query subject.

2. GENERATION OF A PATIENT-SPECIFIC ATLAS

In this paper we demonstrate the creation of atlases specific to a certain measure or feature, for example age, gender or disease. We present a method for the construction of patient-specific atlases of the brain. Traditional atlases of the brain aim to characterize the variability of a population of subjects. A common approach is to map the anatomies of each subject of the population into a common coordinate system and then average these anatomies. During the averaging process each subject is equally weighted.

The resulting atlases are population-specific rather than subject specific. In this paper we propose a method for the construction of patient-specific atlas for a given patient (or

We are grateful to the Swedish Research Council for funding this work.

query subject) from a large population cohort. During the atlas construction we compute the similarity between the query subject and each other subject in the population cohort. This similarity measure can be based on image similarity or other meta-information (e.g. sex, age, ethnicity, pathology). The similarity values between the query subject and the subjects in the population can be used to provide weights that can be used during atlas creation. We present examples where inter-subject similarity is based on their ages.

3. KERNEL SMOOTHING

We use kernel smoothing for the construction of the patient-specific atlases. Kernel smoothing is a standard statistical tool for filtering out high-frequency noise from signals with a lower frequency variation [9]. In this work, we use the technique to obtain time dependent estimates of ventricular and tissue volume for the population and to generate a 4D time varying brain atlas. The technique is used across the population of the training set to compute the average signal for any given age, using weighted support from the examples that are close to the target age. The kernel serves both to interpolate between the examples and to average out the variation due to individual subjects, which is treated as noise.

The path of the average trajectory $x(t)$ is parameterised by the target age, t, and given by

$$x(t) = \frac{\sum_{i=1}^{N} w(t_i, t) y_i}{\sum_{i=1}^{N} w(t_i, t)} \quad , \tag{1}$$

where N is the size of the population, t_i is the age of subject i and y_i is the signal from the corresponding image.

We use the Gaussian kernel, defined by

$$w(t_i, t) = \frac{1}{\sqrt{2\pi}\sigma} e \frac{-(t_i - t)^2}{2\sigma^2}$$

The width of the kernel, σ, is a parameter that is determined by the size of the input dataset and its distribution. Smaller values tend to to introduce noise into the time-varying trajectory since it becomes influenced by individual examples, while values that are too large will tend to smooth out variation in which we are interested. For our data, we found that good results are obtained for $3 < \sigma < 5$.

4. AVERAGE SPACE ATLAS CREATION

The method used for the creation of average space atlases is based on the use of transformation averaging [5, 6, 10]. In this approach, the images to be averaged are registered to a chosen reference and the resulting transformations are averaged to create the atlas. This process is illustrated in Figure 1 where images $\{\mathcal{I}_1, \ldots, \mathcal{I}_n\}$ are registered to the reference image $\mathcal{I}_{ref}$. The resulting transformations, $\{\mathbf{T}_1, \ldots, \mathbf{T}_n\}$, can be averaged to produce $\bar{\mathbf{T}}$, which can generate a set of transformations $\{\mathbf{T}_1\bar{\mathbf{T}}^{-1}, \ldots, \mathbf{T_n}\bar{\mathbf{T}}^{-1}\}$ that are used to spatially normalise the images $\{\mathcal{I}_1, \ldots, \mathcal{I}_n\}$. These are then averaged to produce the atlas $\bar{\mathcal{I}}$. This method of generating average space atlases has been shown to be robust to the choice of reference [6, 10] and representative of the images of the group [11].

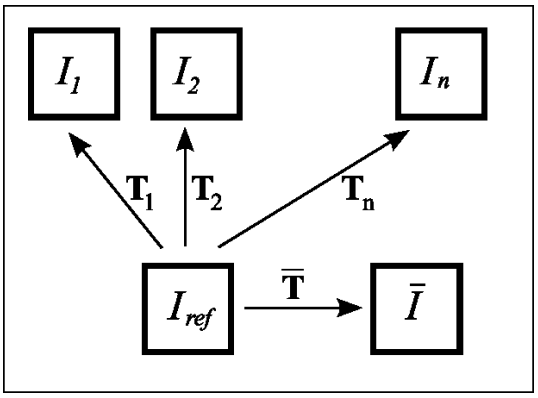

Fig. 1. The average space atlas, $\bar{\mathcal{I}}$, is generated using the inter-subject transformations $\{\mathbf{T}_1, \ldots, \mathbf{T}_n\}$ and their average $\bar{\mathbf{T}}$.

As a pre-processing step, all images were affinely aligned to the reference so that the remaining differences are represented by non-rigid (local) displacements. The intensities of all images were also linearly normalised to have the same mean and standard deviation. The non-rigid registrations were carried out using free-form deformations (FFDs) where vectors at a lattice of control points are blended using B-splines to provide a smoothly varying displacement field [12]. The inter-subject displacements can be averaged using the expression

$$\bar{\mathbf{T}} = \frac{1}{N} \sum_{i=1}^{N} \mathbf{T}_i$$

where the averaging is applied to the control point components. This expression can be extended to incorporate the weights derived from kernel smoothing (Eq. (1))

$$\bar{\mathbf{T}}(\mathbf{x}, t) = \frac{1}{c} \sum_{i=1}^{N} w(t_i, t) \mathbf{T}_i(\mathbf{x}) \tag{2}$$

where c is a normalising constant, $c = \sum_{i=1}^{N} w(t_i, t)$. The average space atlas at time point t can then be given by

$$\bar{\mathcal{I}}(\mathbf{x}, t) = \frac{1}{c} \sum_{i=1}^{N} w(t_i, t) \mathcal{I}_i \circ \mathbf{T}_i \circ \bar{\mathbf{T}}^{-1}(\mathbf{x}) \tag{3}$$

Equations 2 and 3 show that the kernel smoothing weights are used both during the transformation averaging stage and during the creation of the average atlas.

5. RESULTS

5.1. The IXI database

The IXI database is a cross-sectional brain imaging study and contains MR images from 575 normal subjects between the age of 20 and 80 years. For each subject a comprehensive set of MR images are acquired including T1, PD- and T2-weighted volumes, dense "pseudo-volumes" based on acquiring overlapping slices as well as DTI and MR angiograms. Imaging was carried out at three sites on three different scanners (Philips 1.5T, Philips 3T and a GE 3T). All images are anonymised and have been converted to the NIFTI file format. The image data together with meta data that describes the image properties and includes basic demographic information collected from the subjects (age, gender, handedness, smoking habits etc) is freely available for download subject at `http://www.ixi.org.uk`.

In this paper we have only used the T1-weighted MR images. These images have a size of 256 x 256 x 150 with a voxel size of 0.9375mm x 0.9375mm x 1.2mm. All T1-weighted images were bias corrected and segmented into tissue classes using SPM5. After this the images were registered to the MNI template using affine registration. After affine registered the images were registered to non-rigid registration [12].

5.2. Kernel smoothing of the ventricular size, GM- and WM- volume

Regions of interest (ROIs) were defined using the available grey and white matter masks for the Brainweb reference atlas. An additional manual segmentation was generated for the ventricles. Given a transformation from the reference to a subject's image, it is possible to estimate a volume change map in the space of the reference using the Jacobian determinants, $J(\mathbf{x})$, where $\mathbf{x}$ is a reference location. Let Ω be a particular ROI and $\mathbf{T}_i$ be the transformation between the atlas and image i. To measure the size of the Ω in image i an estimate of the volume $|\mathbf{T}_i(\Omega)|$ is needed. This represents the volume of Ω after the transformation is applied and is given by

$$|\mathbf{T}_i(\Omega)| = \sum_{\mathbf{w}\in\mathbf{T}_i(\Omega)} 1 \approx \sum_{\mathbf{v}\in\Omega} J(\mathbf{v})$$

where $\mathbf{v}$ and $\mathbf{w}$ represent reference and subject voxel locations respectively.

In Figure (3) the ventricular volume (normalised by brain size), grey matter volume and the white matter volume are plotted for all the images in the training set over time. The regression curves shown were calculated using kernel smoothing (Eq. (1)) with a value of $\sigma = 4$. For the ventricles, we can see that from the age of 50 the volume of the ventricles start to increase almost linearly with age.

Figure (3) shows a linear decrease in grey matter volume from the age of 25. This matches earlier findings (see [13] for example). It can also be seen in the figure that the white matter starts to decline around the age of 50. From the age of 20 to 50 there seems to be a very slight increase in white matter volume.

5.3. The patient-specific 4D atlas of the ageing brain

Using Eq. (3) we can create an average space atlas at any given time point t. In this way we can create a time-varying 4D brain atlas from the age of 20 to 80. Figure (2) shows images taken at the age 30, 40, 50, 60, 70, 80 from the resulting atlas. A movie illustrating this atlas can be downloaded from `http://www.doc.ic.ac.uk/~anders/movie/`. It can be seen in the images that the anatomy is stable throughout the video, except that the ventricles increase in size.

6. CONCLUSIONS

In this paper we have derived a method for the construction of patient-specific atlas for a given patient (or query subject) from a large population cohort. During the atlas construction we compute the similarity between the query subject and each other subject in the population cohort. This similarity measure can be based on image similarity or other meta-information (e.g. sex, age, ethnicity, medical history, etc). We have shown an example of the construction of brain atlases for different ages using a cohort of 575 subjects between the ages of 18 and 80. This gives us a 4D average space atlas.

Kernel smoothing is used to construct the 4D atlas and to exemplify this method we have done kernel regression on the GM-, WM- and ventricular-volume.

Future work will focus on other similarity measures. One possibility is to calculate the principal components of the free form deformation-transformations and use a Mahalanobis distance on the parameter space as a similarity measure.

7. REFERENCES

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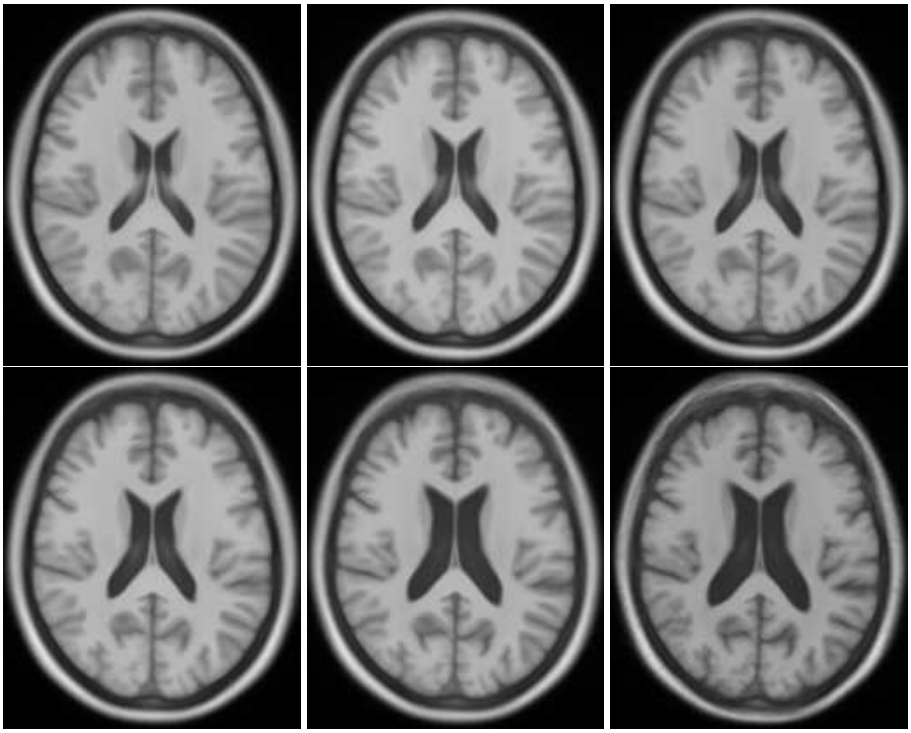

Fig. 2. The images (from left to right) at 30, 40, 50, 60, 70, 80 years old taken from the created movie.

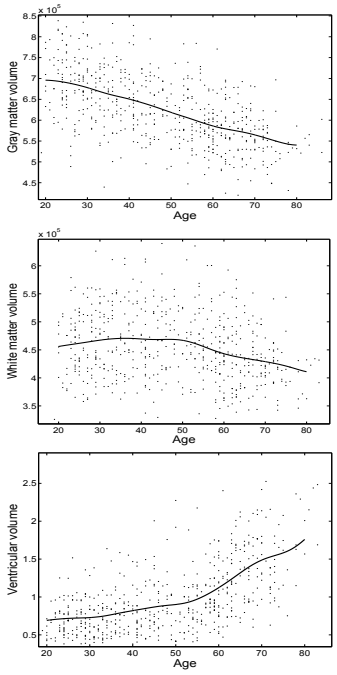

Fig. 3. The grey matter volume (top), the white matter volume (middle) and ventricular volume (bottom).

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